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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,242	04/01/2004	James Freddo	PC25581A	9207

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,242	FREDDO ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-16,32-41,46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-16,32-41, 46 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed **1/24/07** presents remarks and arguments to the office action mailed **11/03/06.** Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 8-16, 32-41, 46 and 49-51 are pending in this office action.

Claims 49-51 are newly added.

References

The new references submitted with the remarks have been received, considered and is acknowledged and the rejections are made in light of the said references.

Maintained Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-41 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating lung cancer cells and or human umbilical vein endothelial cells, does not reasonably provide enablement for treating a wide variation of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Although applicant has amended the claim of abnormal cell growth, there still remain the question of treating cancer which is very broad.

Applicant traverses that the Examiner concludes that in the absence of a correlation between at least some of the disease states claimed as being capable of being treated by the compound of formula I, one of skill in the art would be unable to predict the possible results and that the present claims are not directed to methods of treating cancer using a specific dosage amount to treat cancer and that claims to the treatment of a wide variety of cancers using the specific compound shown in formula I is supported by the specification. In particular, the compound of formula I is noted to be an inhibitor of vascular endothelial cell growth factor receptor (VEGF-R) and of platelet-derived growth factor receptor-13 (PDGFR-13), both of which are targets recognized in the art to be related to angiogenesis and tumor growth (see Bergers, J. Clin. Invest. 111:1287-1295 (2003)- Exhibit 1). Abnormal angiogenesis is a recognized hallmark of several disease states, such as retinopathies, psoriasis, rheumatoid arthritis, age-

related macular degeneration, and cancer (see Folkman, Nature Med. 1:27-31 (1995) - Exhibit 1).

In response, Applicant has not shown how this compound, a single compound of formula I is capable of treating a wide variation of cancer. Although Applicant asserts that the use of anti-angiogenic agents to treat a variety of disease states that rely on angiogenesis is a common strategy in the pharmaceutical arts (see Senger, Am. J. Pathol. 149:1-7 (1996) - Exhibit 1). It is also true that no one drug has been used successfully in the treatment of a wide variation of cancers. The office is aware of the term angiogenesis however, the tumor proliferation is more complex and unpredictable, because of the complex cellular and molecular mechanisms that regulate vessel development in tumors. Angiogenesis can be stopped by a) blocking initial signal from the tumor, b) making initial signal from the tumor less effective, c) stopping the enzyme pathway, d) normalizing mangled blood vessels and e) preventing the switch from turning on. Clearly this one drug does not have the capability of doing performing all of these functions in every cancer. The term treating cancer is very broad.
The argument to angiogenesis is not considered, the claims are to treating cancer, no where is there mentioned the term angiogenesis. Specific drugs are known to treat specific cancers. For example Erbitux for the treatment of colon and head and neck cancers, gefitunib for lung cancer. (see enclosed article www.mayoclinic.com/health/angiogenesis/CA00079.

As to the affidavit for example (pp. 16-39) from an internal report summarizing pre-clinical studies of axitinib indicate that this compound showed significant tumor growth

inhibition in several xenograft mouse models of a variety of cancers, including colon (see pp. 16-21), breast (see pp. 21-24), lung (see pp. 25-28), melanoma (see pp. 28-32), renal cell carcinoma (see pp. 32-33), glioblastoma (see pp. 33-36), and non-Hodkin's lymphoma (see pp. 36-38), Applicant should bear in mind that these are pre-clinical testing a step towards treatment in human, and these findings may or may not be successful in humans.

Argument unpersuasive and rejection is maintained.

In other for the rejection to be withdrawn, specific types of cancers should be cited to limit the scope of the rejected claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kania et al. WO 2001/02369 now a US Patent 6,531,491.

Applicant argues that the cited reference does not teach the claimed dosage forms as recited in the claims and that the claims recite from about 0.001-50 mg/kg.

This argument is traversed. The mere fact that the claims gave the range of dosage clearly indicates that any range within that is capable of been use.

For example for the limitation of instant claim 8, no more than 30 mg, if the patient weighs 70 kg and 0.4 mg per kg is administered it will give 38 mg which is well within the claim limitation and subsequently the ranges can be regulated to fall within the claim limitation of 8-14. The cited rages are anticipated in the references.

Claims 32-41 and 46 rejected under 35 U.S.C. 102(b) as being anticipated by Kania et al. WO 2001/02369 now a US Patent 6,531,491.

Applicant argues that Kania refers to methods of using the compounds disclosed therein for treating various types of cancer. As discussed above, however, this disclosure is provided in a very generic sense with reference to all of the compounds in Kania, and is not specifically directed to the compound of formula I. Furthermore, Kania does not disclose the use of the specific compound of formula I for treating cancer using the specific dosage amounts as recited in the present claims.

In response, this is found un persuasive, the reference teaches the Indazole compounds and pharmaceutical compositions for inhibiting protein kinases, and methods for their use. The compounds of formula IV in the Kanias' reference includes the formula I (see col. 8, lines 35-65). And with regards to the dosage, Kania teaches such as already discussed above, and since for claim 32, is not specify the type of cancer that is required for the dosage ranges, it is anticipated that the reference teaches example claim 32 reads on any variation of cancer cell is anticipated.

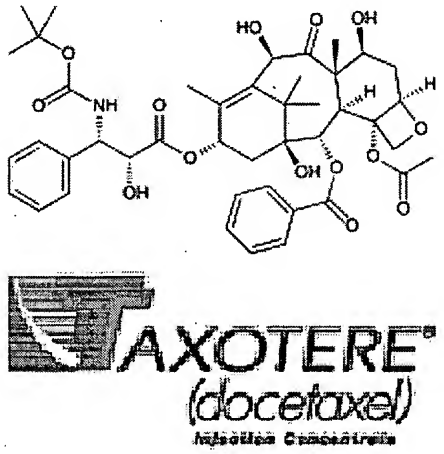
Claim Rejections - 35 USC § 103

Claims 32-41 and 46 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kania et al. WO 2001/02369 now a US Patent 6,531,491.

Examiner has excluded the Sweeney reference as the claims pertaining such have been cancelled and no longer exist.

Applicant argues that no specific teaching is taught with regards to the dosage forms. Kania specifically teaches the dosage forms that optimal dosage for given set of conditions can be ascertained by those skilled in the art (see col. 21, lines 25-30).

In response, with regards to adjuvant therapy, this is not novel, Goodman and Gilman teach that anti cancer drugs can be combined with antineoplastic drugs. Wherein Goodman and Gilman teach adjuvant chemotherapy (see page 1225 and 1230) therefore one of ordinary skill in the art would have been motivated to add an antineoplastic drug to the compound formula I for treatment of cancer. Despite such disclosure or teaching, the Kania reference teaches that he inventive compounds may be used advantageously in combination with other known therapeutic agents. For example, compounds of Formula I, II, III, or IV which possess antiangiogenic activity may be co-administered with cytotoxic chemotherapeutic agents, such as taxotere



Docetaxel

which is the registered name for docetaxel ( ) (see col.13, lines 6-15). Therefor nothing unobvious is seen in using the kanias' reference to arrive at the claim invention. As to claim 46, the Kania reference teaches lung cancer (see col. 275, lines 52-53).

Applicant's arguments filed have been fully considered but they are not persuasive.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-16, 32-41, 46 and 49-51 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1 - 11** of U.S. Patent **7141581**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both applications recite using the same compositions and/or derivatives thereof. See current application claims 8-16, 32-41, 46 and 49-51 and copending application claims 1 – 11. The compositions recited in the claims are anticipatory of each other for the treatment of various types of cancers.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
3/27/07

Ardin H. Marschel 4/2/07
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SUPERVISORY PATENT EXAMINER